

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.

| | | | |
|--|--|-----------|-------------------------------|
| NAME <div style="text-align: center;">Arias, Irwin M.</div> | POSITION TITLE Senior Scientist, Emeritus NIH Two oOther Emeritus Professorships: Einstein and Tufts Albert Einstein College of Medicine (Medicine); Tufts | | |
| eRA COMMONS USER NAME (credential, e.g., agency login) | | | |
| EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)</i> | | | |
| INSTITUTION AND LOCATION | DEGREE <i>(if applicable)</i> | MM/YY | FIELD OF STUDY |
| S.B. Harvard University | (Honors) | 1946 | Protein Chemistry (Honors) |
| Graduate Student-Columbia University, NY | | 1947-1948 | |
| State University of New York, Brooklyn | M.D. | 1952 | |

A. Personal Statement

Through my career as clinician, basic scientist, educator and mentor, I have focused on bridging basic science with medicine. I have studied both basic liver cell biology and clinical liver pathological conditions. My lab's discoveries of mechanisms of inheritable jaundice, and that ABC transporters mediate bile transport; and AMPK and Liver Kinase-B1 regulate hepatocyte polarization and bile transporters, established new paradigms for biliary secretion and molecular identification of inheritable liver diseases. These discoveries not only are important for our understanding of the liver biology, but also have important applications for diagnosis and treatment of liver diseases. My other major accomplishment was in development of programs to train PhD scientists in pathobiology of human disease. In this regard, I have served on many national and international committees, foundations and other organizations concerning basic and translational medical science as well as educational projects.

B. Positions and Honors

| | |
|--------------------------|--|
| 1956 - 1969 | Assistant, Associate Professor, Albert Einstein College of Medicine, Bronx, NY |
| 1956 - 1984 | Attending Physician, Bronx Municipal Hospital Center |
| 1948 - 1968 | Associate Professor of Pharmacology (Visiting), Stanford University |
| 1967 - 1984 | Principal Investigator, USPHS GI Training Program; Director of Program and Chief, Div. of Gastroenterology-Liver Disease, Albert Einstein College of Medicine, Bronx, NY |
| NY 1969 - 1984 (2000) | Professor of Medicine, Albert Einstein College of Medicine, Bronx, NY; Emeritus |
| 1973 - 1984 | Associate Chairman, Department of Medicine, Albert Einstein College, Director, Liver Research Center, Albert Einstein College of Medicine, Bronx, NY |
| 1976 - 1977 | Professor of Chemistry (Visiting) |
| 1982 - 1983 | Scholar in Biochemistry-Molecular Biology (Visiting), Harvard Univ., Cambridge, MA |
| 1984 - 2002 2007 | Prof. & Chairman, Dept. of Physiology, Tufts Univ. Schools of Medicine: Emeritus, |
| 1985 - | Professor, Dept. of Physiology Emeritus, Tufts/New England Medical Center |
| 1985 - | Professor of Medicine (Visiting), Emeritus, Dept. of Medicine, Albert Einstein College of Medicine, Bronx, NY |
| 1986 - 1988 | Fogarty Center Scholar-in-Residence, NIH |
| 2000-2002 | Fogarty Center Scholar-in-Residence, NIH |
| 2007- 2012 | Senior Scientist, NICHD |

2000 - 2012 Assistant to Director, Intramural Program, NIH
 2012`- Senior Scientist, Emeritus NIH

AWARDS AND HONORS:

1958 B.B. Vincent Lyons Award, American Gastroenterologic Association
 1959 E.B. Scripps Institute for Comparative Biology, San Diego-Special Fellowship
 1961 Distinguished Achievement Award, American Gastroenterologic Association
 1961 Distinguished Commendation Medal in Medicine, University of Recife, Brazil
 1963 Annual Honorary Medical Award, University of Chile, Santiago
 1964 Citation in Science, University of Caracas, Venezuela
 1965 Distinguished Achievement Award, American College of Gastroenterology
 1967 Distinguished Achievement Award, Canadian Gastroenterologic Association
 1973 Albert Einstein College of Medicine Annual Distinguished Lecturer
 1982 & 2002 Fogarty Center Scholar In Residence, NIH
 1989 - 1993 University Professor, University of Firenze
 1984 - Scientific Advisory Committees: University of Colorado Liver Research Center and Albert Einstein College of Medicine Liver Research Center
 1987 - 1995 Merit Award, NIDDK, NIH
 1991 Tribute from American Liver Foundation
 1994 Distinguished Achievement Award, AASLD
 1992 Establishment of Irwin M. Arias, M.D. Postdoctoral Fellowship by the ALF
 1995 Honorary degree in Medicine, University of Guadalajara, Mexico
 1996 Tufts University, Distinguished Faculty Award
 1990 Establishment of the American Liver Foundation Annual Irwin M. Arias, M.D. Symposium on "*Bridging Basic Science with Liver Disease*" (currently in 20th year).
 1997 Ukrainian National Research Academy, Honorary Member
 1998 Distinguished Scientific Achievement Award, Asian-Pacific Association for Study of Liver Disease
 1998 Distinguished Scientific Achievement Award, ALF
 1998 Horace Davenport Achievement Award and Lecturer, American Physiological Society
 2004 Named AGA Research Fellowship
 2009 National Academy of Science and Mexican Liver Association, inauguration of Irwin M. Arias, MD Annual Symposium on "*Bridging Basic Science and Liver Disease*"
 2010 Elected as Honorary Member, Mexican National Academy of Science
 2012 Distinguished Achievement Award for an Alumnus, Downstate Medical Center, SUNY
 2015 M.D. Honorary degree University of Astana, Kazakhstan

C. Selected Peer-reviewed Publications

Educational: (of 8 publications)

1. Arias, IM Training basic scientists to bridge the gap between basic science and its application to human disease. New Engl J Med 321: 972-4, 1989
2. Arias, IM Training programs for PhD scientists In *Bridging the Gap*" National Research Council No 0-309-09112, 2004

Selected Science (of 345 publications)

3. Arias, IM. Gartner, LM, Cohen, M, Ben-Ezzer, J, Levi, AJ. Chronic nonhemolytic unconjugated

- hyperbilirubinemia with glucuronyl transferase deficiency: clinical, biochemical, pharmacologic and genetic evidence for heterogeneity. *Amer. J. Med.* 47:395- 409, 1969.
4. Levi, AJ, Gatmaitan, Z, Arias, IM. Identification of two hepatic cytoplasmic proteins, Y and Z, and their possible role in the uptake of bilirubin, sulfobromophthalein and other organic anions. *J. Clin. Invest.* 48:2156-2167, 1969.
5. Kamimoto, Y, Gatmaitan, Z, Che, M, Arias, IM. The function of Gp170, the multidrug resistance gene product, in rat liver canalicular membrane vesicles. *J. Biol. Chem.* 264:11693-11698, 1989.
6. *Nishida, T, Gatmaitan, Z, Che, M, Arias, IM. Rat canalicular membrane vesicles contain an ATP-dependent bile acid transport system. *Proc. Natl. Acad. Sci. USA*, 88:6590-6594, 1991.
7. Kipp, H, Pichetsthot, N, and Arias, IM. Transporters on demand: Intrahepatic pools of canalicular ATP-binding cassette transporters in rat liver. *J. Biol. Chem.* 10:7218-7224, 2001.
8. *Wakabayashi, Y, Lippincott-Schwartz, J, and Arias, IM. Intracellular trafficking of bile salt export pump (ABC B11) in polarized hepatic cells: constitutive cycling between the canalicular membrane and rab-11 positive endosomes. *Mole. Biol. Cell* 15(7): 348596,2004
9. Fu, D, Wakabayashi Y, Lippincott-Schwartz J, Arias IM. Regulation of bile canalicular network formation and maintenance by AMPactivatedprotein kinase and LKB1. *J. Cell Science* 123(19):3294-3302, 2010
10. Fu, D, Wakabayashi Y, Lippincott-Schwartz J, Arias IM. Bile acid stimulates hepatocyte polarization through a cAMP-Epac-MEK/LKB1-AMPK pathways. *Proc. Nat. Acad. Science USA* 108: 1403-8, 2011
11. Ujhazy P, Ortiz D, Misra S, Li S, Moseley J, Jones H, Arias IM. Familial intrahepatic cholestasis 1: studies of localization and function. *Hepatology* 34:768-775, 2001.
12. Kagawa T, Varticovski L, Sai Y, Arias IM. Mechanism by which cAMP activates PI3-kinase and increases bile acid secretion in WIF-B9 cells. *Am J Physiol Cell Physiol* 283:C1655-C1666, 2002.
13. Misra S, Varticovski, L, Arias IM. Mechanisms by which cAMP increases bile acid secretion in rat liver and canalicular membrane vesicles. *Am J Physiol Gastrointest Liver Physiol* 285:G316-G324, 2003
14. Harris MJ, Arias IM. FIC1, a P-type ATPase linked to cholestatic liver disease, has homologues (ATP8B2 and ATP8B3) expressed throughout the body. *Biochim Biophys Acta* 1633:127-131, 2003.
15. Ortiz DF, Moseley J, Calderon G, Swift AL, Li S, Arias IM. Identification of HAX-1 as a protein that binds bile salt export protein and regulates its abundance in the apical membrane of Madin-Darby canine kidney cells. *J Biol Chem* 279:32761-32770, 2004.
16. Mochizuki K, Kagawa T, Numari A, Harris MJ, Itoh J, Watanabe N, Mine T, Arias IM. Two N-linked glycans are required to maintain the transport activity of the bile salt export pump (ABCB11) in MDCK II cells. *Am J Physiol Gastrointest Liver Physiol* 292:G818-G828, 2007.
17. Wakabayashi Y, Chua J, Larkin JM, Lippincott-Schwartz J, Arias IM. Four-dimensional imaging of filter-grown polarized epithelial cells. *Histochem Cell Biol* 127:463-472, 2007.
18. Renz M, Daniels BR, Vamosi G, Arias IM, Lippincott-Schwartz J. Plasticity of the asialoglycoprotein receptor deciphered by ensemble FRET imaging and single-molecule counting PALM imaging. *Proc Natl Acad Sci USA* 109:E2989-E2997, 2012
19. Kipp H, Arias IM. Newly synthesized canalicular ABC transporters are directly targeted from the Golgi to the hepatocyte apical domain in rat liver. *J Biol Chem* 275:15917-15925, 2000.
20. Ujhazy P, Ortiz D, Misra S, Li S, Moseley J, Jones H, Arias IM. Familial intrahepatic cholestasis 1: studies of localization and function. *Hepatology* 34:768-775, 2001.
21. Kagawa T, Varticovski L, Sai Y, Arias IM. Mechanism by which cAMP activates PI3-kinase and increases bile acid secretion in WIF-B9 cells. *Am J Physiol Cell Physiol* 283:C1655-C1666, 2002.
22. Misra S, Varticovski, L, Arias IM. Mechanisms by which cAMP increases bile acid secretion in rat liver and canalicular membrane vesicles. *Am J Physiol Gastrointest Liver Physiol* 285:G316-G324, 2003

23. Harris MJ, Arias IM. FIC1, a P-type ATPase linked to cholestatic liver disease, has homologues (ATP8B2 and ATP8B3) expressed throughout the body. *Biochim Biophys Acta* 1633:127-131, 2003.
24. Ortiz DF, Moseley J, Calderon G, Swift AL, Li S, Arias IM. Identification of HAX-1 as a protein that binds bile salt export protein and regulates its abundance in the apical membrane of Madin-Darby canine kidney cells. *J Biol Chem* 279:32761-32770, 2004.
25. Mochizuki K, Kagawa T, Numari A, Harris MJ, Itoh J, Watanabe N, Mine T, Arias IM. Two N-linked glycans are required to maintain the transport activity of the bile salt export pump (ABCB11) in MDCK II cells. *Am J Physiol Gastrointest Liver Physiol* 292:G818-G828, 2007.18., Wakabayashi Y, Chua J, Larkin JM, Lippincott-Schwartz J, Arias IM. Four-dimensional imaging of filter-grown polarized epithelial cells. *Histochem Cell Biol* 127:463-472, 2007.
26. Fu D, Mitra K, Sengupta P, Jarnik M, Lippincott-Schwartz J, Arias IM. Coordinated elevation of mitochondrial oxidative phosphorylation and autophagy help drive hepatocyte polarization. *Proc Natl Acad Sci USA* 110:7288-7293, 2013.
27. Homolya, L, Fu, D, Sengupta, B, Jarnik, M, Gillet JP, Gitkaind, SJ, Lippincott-Schwartz, J, Arias, IM. LKB1/AMPK and PKA control ABCB11 trafficking and polarization in hepatocytes. *PLOS One* 9(3); 1-16, 214.
28. Erlanger, S, Arias, IM, Dhumeaux, D. Inherited disorders of bilirubin transport and conjugation: new insights into molecular mechanisms and consequences. *Gastro*. 146:1625-1638, 2014
29. Gissen, P, Arias, IM. Hepatocyte polarity: mechanisms and liver disease. *J. Hepatology* 2015
30. Porath-Shliom, N, Janik, M, Anderson, JM, Gutkind, S., Weigert, R, Arias IM. LKB1 regulates hepatocellular tight junction distribution and function in vivo. (in review).

Other publications: author or Editor of 12 books...most recent 5th edition of *The Liver* Biology and Pathobiology Wiley-Blackwell Press, 2010; 12 editorials and 47 invited chapters and reviews.

In addition:

Founding Editor of *Hepatology*, official journal of the American Association for Study of Liver Disease

36 former Fellows have become Professors; many of whom direct Liver Research Centers around the world.

Director of named American Liver Foundation Symposium ("Bridging Basic Science and Liver Disease") now in its 26th year